

REMARKS

Claims 22-57 are currently pending in this application. Applicants have cancelled claims 1-21 and added new claims 22-57. New claims 22-57 are generally supported by the cancelled claims and throughout the specification. For example, claim 22 is supported by cancelled claim 10 and the passage at page 22, line 30 to page 23, line 1. Claims 23, 26, 28, 31, 33 and 36 are supported by cancelled claim 13 and the passages at page 10, lines 16-22 and at page 21, lines 13-20. Claims 24, 29 and 34 are supported by cancelled claim 3 and the passage at page 11, lines 23-28. Claims 25, 30 and 35 are supported by cancelled claim 15 and the passage at page 25, lines 7-11. Claim 27 is supported by cancelled claim 14 and the passage at page 23, line 22 to page 23, line 7. Claim 32 is supported by the passage at page 19, lines 8-21. Claims 37, 41, 42, 46, 47 and 51 are supported by the passages at page 2, lines 2-11; page 24, line 29 to page 25, line 6; page 52, lines 16-20; and page 53, lines 5-13. Claims 38, 43, and 48 are supported by cancelled claim 17 and the passage at page 25, line 30 to page 26, line 4. Claims 39, 44, and 49 are supported by cancelled claim 18 and the passage at page 25, lines 20-29. Claims 40, 45, and 50 are supported by cancelled claim 19 and the passage at page 25, lines 29-30. Claims 52-54 are supported by cancelled claim 20 and the passage at page 25, lines 10-15. Claims 55-57 are supported by cancelled claim 21 and the passage at page 26, lines 12-21. Applicants have also amended the specification to correct a number of typographical errors.

The above amendments are submitted without waiver or prejudice to Applicants' ability to pursue any cancelled subject matter in any continuing patent application. Reconsideration of the application, as amended, is respectfully requested.

Specification

The Examiner requested that the lengthy specification needs to be checked and corrected. See the Office Action, page 2, lines 6-8. Applicants met the request.

Claim objections

The Examiner objected to claims 2-9, 11-13, and 17-19 for beginning with “A method” instead of “The method.” See the Office Action, page 2, lines 10-12. Applicants have cancelled these claims. New claims 22-57 do not suffer from this deficiency.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 7, 11, 13, and 16-19 for being indefinite on various grounds. See the Office Action, page 2, lines 17-19. Applicants have cancelled these claims.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1, 3, 8, 10, 12, and 14-21 as being unpatentable over Yamada et al. (JP 09-297137) in view of Lang et al. (EP 0 617 289). According to the Examiner, it would have been obvious to one of ordinary skill in the art to combine the lyophilization described in Lang et al. with the process of denaturing lipoprotein described in Yamada et al. See the Office Action, page 5, lines 5-8. Applicants respectfully disagree.

Claims 1, 3, 8, 10, 12, and 14-21 have been cancelled. New claims 22, 24, 25, 27, 29, 30, 32, 34, 35, and 37-57 corresponding to cancelled claims 1, 3, 8, 10, 12, and 14-21 have been added. The subject matters covered by these new claims include a method of denaturing lipoprotein by freezing and subsequent melting (e.g., claim 22); denatured lipoprotein produced by this method (e.g., claim 25); a method of stabilizing thus-obtained denatured lipoprotein by freeze-drying or lyophilization (e.g., claim 27); a method of stabilizing thus-obtained denatured lipoprotein by adding a stabilizer prior to freeze-drying (e.g., claim 32); a method of determining thus-obtained denatured lipoprotein in a sample by selecting it as a standard and reacting and binding it with an antibody, measuring the reactivity of the antibody, and comparing the reactivity with a calibration curve (e.g., claim 37); and a reagent kit for determining thus-obtained denatured lipoprotein (e.g., claim 52). Claims 24, 25, 27, 29, 30, 32, 34, 35, 37-57 share the common feature of denaturing lipoprotein by freezing and subsequent melting.

Yamada et al. discloses a method for denaturing lipoprotein by oxidation, reduction, disruption, heating or modifying agent. It does not disclose the method of denaturing lipoprotein by freezing and subsequent melting.

Lang et al. discloses lyophilization of natural lipoprotein.<sup>1</sup> It also does not disclose a method for denaturing lipoprotein by freezing and subsequent melting.

As Yamada et al. or Lang et al. does not disclose denaturing lipoprotein by freezing and subsequent melting, nor does their combination. In addition, Applicants submit a declaration by Dr. Hiroaki Kohno (attached hereto as "Exhibit A"). The declaration provides data that distinguishes the denatured lipoprotein produced by freezing and subsequent melting from the denaturing lipoprotein produced by oxidation, acetylation, saccharification, and treatment with 4-hydroxy nonenal. In view of the above, Applicants respectfully request the withdrawal of the rejection.

The Examiner rejected claims 2, 6, 11, and 13 as being unpatentable over Yamada et al. in view of Lang et al., and further in view of Kimura et al. (JP 09-288106). According to the Examiner, "[i]t would have been *prima facie* obvious to use human lipoprotein, use denatured lipoprotein as a standard, and the specific antibody of Kimura et al. with the method of Yamada et al. and Lang et al. ...with a reasonable expectation of success." See the Office Action, page 6, lines 3-6. Applicants respectfully disagree.

Claims 2, 6, 11, and 13 have been cancelled. New claims 23, 26, 28, 31, 33, 36, 41, 46, and 51 corresponding to cancelled claims 11 and 13 have been added. Claims 23, 26, 28, 31, 33, 36, 41, 46, and 51 share the common feature of denaturing lipoprotein by freezing and subsequent melting.

Kimura et al. does not disclose a method for denaturing lipoprotein by freezing and subsequent melting. As discussed above, neither does Yamada et al. or Lang et al. Thus, the Examiner's reliance on these three references to establish a *prima facie* case of obviousness is clearly misplaced. Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claim 9 as being unpatentable over Yamada et al. in view of Lang et al., and further in view of Hallahan et al. (U.S. Patent No. 5,969,040). See the Office Action, page 6, lines 9-11. Applicants have cancelled claim 9.

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<sup>1</sup> By contrast, claim 27 requires lyophilization of denatured lipoprotein, not natural lipoprotein.

Applicant : Takashi Shigematsu et al.  
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The Examiner rejected claim 7 as being unpatentable over Yamada et al. in view of Lang et al., and further in view of Kondo et al. (U.S. Patent No. 6,248,545). See the Office Action, page 6, lines 18-20. Applicants have cancelled claim 7.

The Examiner rejected claims 4 and 5 as being unpatentable over Yamada et al. in view of Lang et al., and further in view of Aviram et al. (U.S. Patent No. 6,362,236). See the Office Action, page 7, lines 7-9. Applicants have cancelled claim 4 and 5.

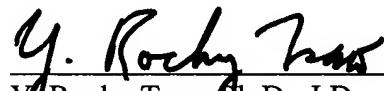
### CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and that claims 22-57 as pending, define subject matter that is patentable. On this basis, it is submitted that all claims are now in condition for allowance, an action of which is requested.

Enclosed is a \$750.00 check for excess claim fees. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney's Docket No. 13723-002001.

Respectfully submitted,

Date: 12-30-04

  
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